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Award Number: DAMD17-01-1-0334

TITLE: Genetic Factors in Breast Cancer: Center for Interdisciplinary Biobehavioral Research

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New York, NY 10029-6574

REPORT DATE: October 2005

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
01-10-2005	Annual	15 Sep 04 – 14 Sep 05

4. TITLE AND SUBTITLE
Genetic Factors in Breast Cancer: Center for Interdisciplinary Biobehavioral Research

5a. CONTRACT NUMBER

5b. GRANT NUMBER
DAMD17-01-1-0334

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Mount Sinai School of Medicine
New York, NY 10029-6574

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Abstract is attached at following page.

15. SUBJECT TERMS
No subject terms provided.

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU	35	19b. TELEPHONE NUMBER *(include area code)*

ABSTRACT

The central goal of the Breast Cancer Behavioral Center is to further our understanding of the impact of biobehavioral factors on genetic aspects of breast cancer in African-American women. The Center has three aims: 1) To support an integrated, interdisciplinary, Program of Research consisting of three synergistic Research Projects (with 4 supporting Cores), each of which addresses an important cancer topic and includes psychological and/or behavioral issues. Thus, we have research projects with implications for breast cancer etiology, behavioral issues, and their interaction; 2) To encourage the development of interdisciplinary thinking among the faculty involved in the Program of Research that can serve as a model for other institutions. Thus, we are demonstrating, by example, the utility of an interdisciplinary approach by working together on an integrated project that addresses important issues of interest to all members of the research team. We propose to bridge the gap between biobehavioral research and epidemiologic approaches. 3) To facilitate the development of truly interdisciplinary perspectives among new investigators in breast cancer research. Thus, we provide interdisciplinary training through both didactic and "hands-on" research, as well as informal seminars to outstanding young investigators who represent the future of the field.

Table of Contents

REPORT OVERVIEW

Annual Award Number DAMD17-01-1-0334

Center Grant Overall Report

Project 1 Report

Project 2 Report

Project 3 Report

Core A Report

Core B Report

Core C Report

Code D Report

CENTER GRANT

Genetic Factors in Breast Cancer:
Center for Interdisciplinary Biobehavioral Research

Behavioral Center of Excellence Award:
Genetic Factors in Breast Cancer:
Center for Interdisciplinary Biobehavioral Research

Principal Investigator: Dr. Dana H. Bovbjerg

INTRODUCTION:

The central goal of the Breast Cancer Behavioral Center of Excellence in the Department of Oncological Sciences of the Mount Sinai School of Medicine is to increase our understanding of the impact of biopsychosocial factors on genetic aspects of breast cancer in African-American women. These women, while on average less likely to get breast cancer than Caucasian women, are more likely to die of the disease. The causes of this health disparity are not yet known, but are likely to involve a complex interplay between genetic factors and biopsychosocial factors at cellular, personal and societal levels. The Behavioral Center's interdisciplinary research efforts to explore this complex topic are grounded in the biobehavioral model of health and disease. According to this theoretical perspective, what people think and feel affects the state of their health in at least two basic ways: 1) by affecting their behavioral choices (e.g., including those for primary prevention (e.g., alcohol consumption), secondary prevention (e.g., following cancer screening guidelines) and tertiary prevention (e.g., following treatment schedules)), and 2) by affecting their biological processes (e.g., increased cortisol levels with stress), each of which is controlled by the central nervous system. A better understanding of the role of biobehavioral factors on the genetic aspects of breast cancer in African American women may have profound implications for cancer prevention and control, as it may suggest novel strategies to reduce the threat posed by this disease to this underserved population.

The Behavioral Center has three primary Objectives: 1) To support an integrated, interdisciplinary Program of Research consisting of three synergistic Research Projects each of which addresses an important issue in breast cancer genetic research with African American women that entails critical psychological or behavioral issues. Thus, our first purpose is to do outstanding research, with implications for our understanding of the etiology of breast cancer, as well as for our understanding of behavior per se. 2) To encourage the development of truly interdisciplinary thinking among the faculty involved in the Program of Research that can serve as a model for other institutions. Thus, our second purpose is to show by example, not only the utility of an interdisciplinary approach (synergy with Objective 1), but one approach that may facilitate its achievement - working together on an integrated project that addresses important issues of interest to all members of the research team. We propose to bridge the gap between biobehavioral research and epidemiologic approaches. 3) To facilitate the development of truly interdisciplinary perspectives among new investigators in breast cancer research. Thus, our third purpose is to provide both interdisciplinary training through both didactic and "hands-on" (synergy with Objective 1) research, as well as informal seminars (synergy with Objective 2) to outstanding young investigators likely to represent the future of the field.

The Program of Research consists of three synergistic Projects (and four supporting Cores), each of which are reported upon separately below.

The three Projects MSSM Center apply the biobehavioral perspective to three distinct loci where such factors are likely to impact genetic issues in breast cancer:

- Project 1, "Behavior, estrogen metabolism, and breast cancer risk: a molecular epidemiologic study" (Ambrosone, PI)--Psychological and behavioral factors are investigated as potential etiological agents in the development of breast cancer, operating through interactions with underlying genetic factors.
- Project 2, "Impact of culturally tailored counseling on psychobehavioral outcomes and BRCA decision making among women with breast cancer" (Valdimarsdottir, PI)--Cultural, psychological and behavioral factors are investigated for their potential impact on patients' decisions regarding genetic testing for breast cancer susceptibility.
- Project 3, "Immune surveillance, stress, and inherited susceptibility to breast cancer: a psychobiological analysis of the healthy daughters of breast cancer patients" (Bovbjerg, PI)--Psychological and behavioral factors are investigated as sources of variability in phenotypic expression of possible biological pathways involved in familial risk of breast cancer, such as immune surveillance mechanisms.

All three Projects are synergistic with one another both theoretically and practically (e.g., Project 1 serves as entry point for participants for Projects 2 & 3) and each Project uses all of the Cores, which are dedicated to:

- Core A, Recruitment, Tracking, and Interviewing;
- Core B, Molecular Diagnostic and Research;
- Core C, Biostatistics and Data Management;
- Core D, Training.

In addition to supporting the three original projects, the Center has also served as a catalyst for the development of several related research studies, now funded by independent DOD Idea awards, that interact both intellectually (shared measures) and practically (shared participants) with the projects in the Center. Most recently the Center has played an instrumental role in the development of another DOD funded Center at Columbia University Medical College, providing intellectual input (Bovbjerg and Ambrosone are co-investigators) and critical practical support. The Behavioral Center will be the primary referral source of recently diagnosed African-American breast cancer patients that are the focus of the new cohort study, and will provide previously collected data (e.g., family history information) for the proposed analyses.

Further understanding of the role of biobehavioral factors on the genetics of breast cancer in African American women may have profound implications for cancer prevention and control, as it may suggest novel strategies to reduce the threat posed by this disease to this underserved population.

BODY:

We received official notification of approval of the HSRRB of the USAMRAA for all of the proposed three Projects in April 2004. Thus we were able to begin recruiting for all three projects. However, because of the delay in receiving approval, we are still substantially behind our anticipated timeline for completion of the tasks listed in the Statements of Work for each of the Projects and Cores (as detailed for each Project and Core in separate sections below). In

June, 2005, we submitted a Request for Supplemental Funding in order to: 1) bring to fruition the three integrated projects originally supported by the Center; 2) enable the full multiplier effect of the Center on three related, independently funded DOD studies (Idea Awards); and 3) ensure the success of a newly funded DOD Center of Excellence at Columbia University Medical Center examining racial disparities in the initiation and intensity of adjuvant therapy for breast cancer. We were granted a two-year extension (Amendment # P00004).

KEY RESEARCH ACOMPLISHMENTS:

At this point in the research, while data collection is ongoing, results are not yet available. See detailed responses for each Project and Core below.

REPORTABLE OUTCOMES:

BC009027 (Neugut, PI) 03/1/05-02/28/10 10%
DOD (Bovbjerg, Site-PI) Direct Costs (MSSM): Current Yr: $154,155/ Total: $781,643
Project Title: "*Causes of Racial Disparities in the Optimal Receipt and Compliance with Adjuvant Systemic Therapy for Breast Cancer*"

CONCLUSIONS:

The results of this research will provide further understanding of the role of biobehavioral factors on the genetics of breast cancer in African-American women. They may thus have profound implications for cancer prevention and control, as they may suggest novel strategies to reduce the threat posed by this disease to this important underserved population. See detailed responses for each Project and Core below.

REFERENCES:

None

APPENDICES:

None

PROJECT 1

Behavior, estrogen metabolism, and breast cancer risk: a molecular epidemiologic study

Project 1:
Behavior, estrogen metabolism, and breast cancer risk:
a molecular epidemiologic study

Principal Investigator: Dr. Christine Ambrosone

INTRODUCTION:

African-American women are more often diagnosed with breast cancer at an early age and have more aggressive disease. They are also more likely to experience menarche at an earlier age and to have higher estrogen levels. We hypothesize that earlier, more aggressive disease is related to earlier menarche and to lifetime hormonal exposures. Both breast cancer and early menarche are likely to be related to behavioral and reproductive factors, and to individual differences in hormone production and metabolism. In a case-control study, we will explore relationships between risk of breast cancer and a number of risk factors that will affect hormonal levels in women. We will also study how those factors may affect age at menarche. Because there is evidence that stressful events in early childhood result in early menarche, we will also evaluate the impact of childhood events on onset of menses. We also will study whether earlier menarche and factors related to greater lifetime exposure to estrogens will be associated with earlier age at breast cancer diagnosis and markers of more aggressive disease. Therefore, we will evaluate relationships between breast cancer risk and lifetime physical activity patterns, alcohol consumption, smoking, diet, weight and weight change throughout the life, early life events, and hormonal and reproductive factors, with data collected through an in-person interview. We will also evaluate genetic differences in hormone metabolism. The same factors, childhood body size, physical activity and early stressful events will also be evaluated in relation to age at menarche. In a case control study, we will identify 800 African-American women with incident breast cancer at hospitals in NYC with the largest referral patterns for African Americans and 800 controls using random digit dialing. In-person interviews will be conducted and a blood specimen drawn. Statistical analyses will be performed to address each of the aims. There are few data to explain the earlier incidence of breast cancer and more aggressive disease among African Americans, and results from this study will elucidate the probable link between breast cancer risk, early age at menarche and hormonal milieu, and the factors that predict them. This molecular epidemiologic study will take into account the role of behavioral factors and early childhood lifetime events in breast cancer etiology, which has not been explored to date.

BODY:

Statement of Work

Task 1. Start-up and organizational tasks:

a. Develop study protocols for ascertainment of cases at each site
b. Identify, hire, and train interviewers
c. Pilot test study questionnaire and refine accordingly
d. Develop other study-related instruments and data collection forms
e. Design database for subject tracking and data entry of questionnaire and other data collection forms, incorporate logic and validity checks

As per last year's report, Task 1 has been completed.

Task 2. Identify and recruit study subjects:

a. Identify ~1,400 incident breast cancer cases at participating hospitals through daily or weekly contact with institutions or private doctor's offices
b. Verify case eligibility and obtain physician consent to contact cases
c. Identify ~1,200 controls through the use of random digit dialing for those 20 to 64 years of age and Health Care Finance Administration roosters for those 65 to 74 years of age
d. Assign unique identification number to each potential participant to be used on all study materials (to ensure confidentiality, personal identifiers will be kept separate from all other data)
e. Mail introductory letter
f. Telephone contact of potential subjects
    1) Introduce study
    2) Schedule in-person interview at a time and place that is convenient for participant

Task 3. Conduct in-person interview:

a. Obtain informed consent and signed medical release form
b. Interviewer administers:
    1) Main questionnaire
    2) Block food frequency questionnaire
c. Measure height, weight, waist and hip circumference
d. Collect blood specimens

Since receiving HSRRB approval on April 16th, 2004, we have been working to put the approved protocol through the IRBs of collaborating hospitals. Final HSRRB approval of these documents is still pending. We have also modified our methodology for patient ascertainment to comply with newer IRB and HIPAA regulations. Because of patient confidentiality issues, we can no longer receive identifiers from physicians. Rather, we will communicate regularly with physician offices and when patients are scheduled who the clinicians feel would be eligible for the study, a research assistant (RA) will be informed, and be present in the clinic on those days. The physicians then receive patient permission for referral to our RA, who will inform potential participants about the study. Alternatively, physicians will refer eligible patients who have granted permission to be contacted by a member of our study team. Contact information for patients who agree to participate in the study will be given to interviewers, who schedule appointments to conduct the informed consent process, administer the interview, perform anthropometry measurements, and collect a blood specimen. Interviews will be conducted at either the patient's home or at the hospital, depending upon their preference.

We have initiated identifying potential controls through random digit dialing. Those who agree to be contacted are sent a letter and brochure and a call is made subsequently to provide further information regarding the study and to schedule an appointment. The interview process is conducted in the same manner as that outlined for cases.

In order to explore the mechanisms of black/white differences, we recently sought and obtained funding from the NCI to build upon the infrastructure of this award and to enroll Caucasian women in NYC and New Jersey and additional African-American women, for a total of 1200 cases and 1200 controls of each race. The protocol and study questionnaire for these awards are the same. In Year 4, we amended the protocol and consent forms to include Caucasians so that they may be recruited simultaneously (amendment received by HSRRB November 2004). This amendment was approved by the HSRRB on April 8, 2005.

Because of all of the work involved in revising the protocols and consents to increase the numbers of African Americans and to include Caucasians, we have not enrolled as many cases and controls as we had anticipated. This year, we have collected data on 140 participants. However, pending approval of the additional hospitals and expansion of our study catchment area, we expect that our numbers will greatly increase.

Task 4. Interviewer quality control:

a. Review the first batch of interviews (n~10) by each interviewer and provide feedback to each interviewer
b. Review all interview-related materials for completeness and internal consistency
c. Provide feedback to interviewers on a regular basis
d. Call back a ten percent sample of both cases and controls to validate questionnaire administration and key information collected

Task 5. Abstract pathology and breast cancer treatment information:

a. Abstract tumor specific characteristics such as tumor size, stage, grade, nodal involvement, and hormone receptor from pathology reports
b. Abstract breast cancer related treatment including surgery and prescribed adjuvant therapies from medical records and physicians' patient files

Task 6. Data entry:

a. Information obtained throughout the study (participant contact information, main questionnaire, pathology and treatment abstract form, body size measurements) will be entered as collected
b. All data will be double key entered to ensure accuracy

Task 7. Food frequency questionnaire data processing:

a. Food frequency questionnaires are sent for scanning and nutrient analysis
b. Data files containing raw data and nutrient information are returned to Mount Sinai on a disk

We have begun to review questionnaires with interviewers and to abstract medical record information for enrolled patients. Data are entered under the direction of Core C (see separate report, below), after questionnaires are reviewed and coded by two RAs.

Task 8. Perform genotyping (Core B):

Blood samples are being collected and DNA extracted. DNA will be banked until the completion of data collection at which time genotyping will be performed.

Task 9. Data cleaning, statistical analysis, and manuscript preparation:

a. Write logic checks to determine out-of-range variable values and inconsistencies
b. Comprehensive analyses of data
c. Drafts of manuscripts
d. Manuscripts submitted

Data collected are being 'cleaned' by investigation of outliers, etc., and programming performed for appropriate transformation of variables from questionnaire data by Core C (see report, below). As yet, we have no results from our study, since data collection is ongoing.

KEY RESEARCH ACCOMPLISHMENTS:

Refine infrastructure for molecular epidemiologic study (questionnaire, protocols and equipment for blood processing and specimen banking, interviewing, hiring, and training interviewers, databases for participant tracking). Identify eligible patients and controls; conduct interviews, process and bank specimens; continue DNA extractions; code questionnaires and enter data.

REPORTABLE OUTCOMES:

We have no reportable outcomes at this time.

CONCLUSIONS:

At this time, we are continuing to enroll participants into the study at the approved hospitals and await approval from HSRRB to recruit at several additional hospitals. No analyses have been performed. Thus, no findings can be reported at this time.

REFERENCES:

None

APPENDICES:

None

PROJECT 2

Impact of culturally tailored counseling on psychobehavioral outcomes and BRCA decision making among women with breast cancer

Project 2:
Impact of culturally tailored counseling on psychobehavioral outcomes and BRCA decision making among women with breast cancer

Principal Investigator: Dr. Heiddis Valdimarsdottir

INTRODUCTION:

Between 5-10% of all breast cancer cases are inherited and demonstrate clear patterns of dominant transmission. These syndromes of breast cancer susceptibility have been linked to mutations in at least two genes, BRCA1 and BRCA2. Individuals with mutations in BRCA1/2 have a 40% to 85% cumulative risk of developing breast cancer and a 5% to 60% cumulative risk of developing ovarian cancer. The decision to undergo genetic testing for breast cancer susceptibility is complex, as women have to evaluate the many potential benefits (e.g., increased surveillance if a woman is found to be a mutation carrier) and risks (e.g., increased distress if a woman is found to be a mutation carrier) associated with genetic testing. An important goal of genetic counseling is to improve knowledge and comprehension about these benefits and risks that are involved in genetic testing. However, research in genetic counseling has shown that many counselees have difficulty comprehending probability information. Some studies of genetic counseling have demonstrated gains in knowledge. However, in that research, as many as one-half of the counselees were no better informed after their counseling. Lerman et al. demonstrated increased knowledge of BRCA1/2 testing following genetic counseling; however, the average knowledge scores were only 65% at the one-month follow-up assessment, with African-American women having the smallest increases in knowledge. These results may not be surprising as African-American women have been found to have less prior knowledge and information about genetic testing than other women. Lerman et al. reported that education and counseling increased the probability that African-American women banked a blood sample for BRCA testing, but this was not the case for Caucasian women. However, our research indicates that although African-American women may be willing to provide blood samples for genetic testing, 20% of them may decline to receive their test results once they are available. This is significantly higher than the 2% refusal rate that we have observed for Caucasian women. These findings raise the possibility that African-American women may experience decisional conflict with regard to testing even after they have undergone standard genetic counseling. One explanation for these findings may be that standard genetic counseling does not specifically address the unique concerns and attitudes that African-American women have about genetic testing. As reviewed in detail in the body of the grant, there is evidence that culture-specific variables play an important role in BRCA-decision making. For example, Hughes et al. reported that compared to Caucasian women, a greater proportion of African-American women endorsed the following items as risks of BRCA testing: a) death from cancer is inevitable, b) modern medicine is not trustworthy, c) testing would be too difficult to handle emotionally, and d) testing might have a significant effect on family members. Another potential barrier to genetic testing among African Americans may be mistrust of the medical community, as African-American women have reported that suspicion influences their medical decisions in general. Genetic counseling that addresses these unique concerns may be more effective in reducing distress associated with testing which, in turn, may increase the likelihood that the counseling

will be effective in increasing knowledge about genetics. Increasing knowledge about genetics may not only increase the probability that women make an informed decision with regard to testing, but it may also affect their attitudes toward surveillance and preventive options as well as increase the likelihood that they will talk to their family members about their breast cancer risk.

The goal of the proposed research is therefore to develop and evaluate the impact of culturally tailored genetic counseling on patient decision making regarding BRCA testing and subsequent cognitive, emotional, and behavioral outcomes. African-American women whose family histories of cancer are suggestive of a hereditary breast/ovarian cancer syndrome will be randomized to receive either Standard Genetic Counseling (SGC) or Culturally Tailored Genetic Counseling (CT-GC). As the CT-GC addresses culture specific benefits and barriers to breast cancer susceptibility testing, we hypothesize that women in the CT-GC group will: 1) be more likely to elect the option that is most consistent with their personal preference; 2) report greater decisional satisfaction and less decisional conflict; 3) report less distress which, in turn, will enhance retention of knowledge and information provided in the counseling session; 4) report stronger intentions to adhere to screening guidelines and to participate in prevention options; and 5) be more likely to disseminate information provided in the counseling to their first-degree relatives.

BODY:

In the past year, we have received HSRRB approval from the Department of Defense. We received approval to extend recruitment to involve women outside of Project 1, including women who are unaffected by cancer, but whose family histories are suggestive of a hereditary breast or ovarian cancer syndrome. Towards that end we are contacting and explaining the study to surgeons and oncologists at local hospitals as well as support groups. We have also contacted other genetics centers in the region to encourage them to refer patients to this study. There is a great interest in the study and willingness to refer women to the study.

Of note, randomization in this study was changed from a 1:1 chance of randomization into the experimental arm, to a 2:1 chance, meaning 1/3 of participants will be randomized to receive standard genetic counseling and 2/3 will receive culturally tailored counseling. This change was implemented because a larger recruitment is needed into the intervention arm in order to better examine potential mediators and moderators of the culturally tailored intervention. This change was approved by both the MSSM IRB and HSRRB.

KEY RESEARCH ACCOMPLISHMENTS:

In this past project year, we have collected data on 24 women.

REPORTABLE OUTCOMES:

We have no reportable outcomes at this time.

CONCLUSIONS:

To date, the culturally tailored counseling protocol has been developed and we have data on 24 women in this grant year.

REFERENCES:

None

APPENDIX:

None

PROJECT 3

Immune surveillance, stress and inherited susceptibility to breast cancer: a psychobiological analysis of the healthy daughters of breast cancer patients

Project 3:
Immune surveillance, stress, and inherited susceptibility to breast cancer: a psychobiological analysis of the healthy daughters of breast cancer patients

Principal Investigator: Dr. Dana H. Bovbjerg

INTRODUCTION:

Mutations in the autosomal dominant breast cancer susceptibility genes (BRCA1/BRCA2), account for less than half the attributable increased risk of breast cancer among first degree relatives of breast cancer patients. This study uses a longitudinal study design comparing the daughters of Cases (N=150) to the daughters of Controls (N=150) in Project 1 to examine the possibility that inherited deficits in immune surveillance mechanisms (e.g., natural killer cell activity, cytokine production) may account for the residual familial risk that cannot be attributed to mutations. In addition, the study explores the contribution of stress-induced immune modulation and inheritance of polymorphisms in the genes coding for two key cytokines, interferon gamma and tumor necrosis factor alpha, to the low surveillance phenotype. The specific aims for this study are: 1) To examine the possibility that variability in the strength of immune defenses may be associated with familial risk of breast cancer; 2) To determine the immunomodulatory effects of concurrently assessed stress responses and behavioral variables; 3) To investigate the possibility that the reductions in NK cell activity associated with familial risk of breast cancer may reflect a broader pattern of inherited alterations in key cytokine pathways; and 4) To conduct an exploratory analysis of the possibility that Case-daughters' levels of stress may be affected by their mothers' participation in genetic counseling. Each participating daughter is assessed (Core A) on two separate occasions approximately 3 months apart at the same time of day. At each assessment standardized self-report measures are completed and, following at least 20 minutes of quiet rest, a blood sample collected. Blood samples are assayed for immune function and cytokine genotypes (Core C). Routine statistical analyses (Core B) will test study hypotheses after anticipated sample sizes are achieved. If the results of the proposed research are consistent with the hypothesis that deficits in immune surveillance contribute to familial risk above and beyond effects of stress, the study could have profound implications for the eradication of breast cancer. Such results would raise the possibility that appropriate interventions to increase the activity of immune surveillance mechanisms in daughters at familial risk, including reduced stress-induced immune suppression, might delay the onset or even prevent the development of breast cancer.

BODY:

We received approval HSRRB approval from the Department of Defense for this study in November, 2004. We received approval to extend recruitment to include daughters of women who may not have participated in Project 1 ("Behavior, estrogen metabolism and breast cancer risk: A molecular epidemiologic study"), but who would have been eligible for the study. We also modified the exclusion criteria to reduce the possibility of selection bias in the study sample.

To reduce participant burden, the protocol was amended to exclude the collection of blood pressure and heart rate data; instead, cortisol levels in self collected saliva samples will be used

to provide an independent assessment of stress. In addition, saliva/buccal cell collection is offered as a less invasive alternative to participants who are unable to provide a blood specimen. Anthropometric measures were added to the protocol in the form of body composition analysis using a Tanita scale and waist and hip measurements.

Statement of Work:

- Task -1 Successful application for HSRRB approval through the USAMRAA office
- Task 1 Setting up of Project 3 procedures
- Task 2 Screening and recruitment of study participants
- Task 3 Inclusion of study subjects
- Task 4 Second assessment of study subjects
- Task 5 Data processing
- Task 6 Statistical analysis

With HSRRB approval in place, in the past year we have completed tasks -1 and 1, getting HSRRB approval and setting up study procedures. With the help of Core A, we have begun tasks 2 and 3, screening, recruiting and interviewing study subjects. In consultation with Core C, we have begun task 5, setting up systems for data entry and cleaning.

KEY RESEARCH ACOMPLISHMENTS:
In this grant year, we have collected data for Project 3 from 15 women.

REPORTABLE OUTCOMES:
We have no reportable outcomes at this time.

CONCLUSIONS:
At this point in the research, no results are yet available. If the results of the proposed research are consistent with the hypothesis that deficits in immune surveillance contribute to familial risk above and beyond effects of stress, the study could have profound implications for the eradication of breast cancer. Such results would raise the possibility that appropriate interventions to increase the activity of immune surveillance mechanisms in daughters at familial risk, including reductions in stress-induced immune suppression, might delay the onset or even prevent the development of breast cancer.

REFERENCES:
None

APPENDICES:
None

CORE A

"Recruitment, Tracking and Interviewing Core"

CORE A:
Recruitment, Tracking and Interviewing Core

Principal Investigator: Lina Jandorf, M.A.

INTRODUCTION:

This Core has the responsibility of contacting the identified cases, controls, and healthy adult daughters of the cases and controls, for participation in the three projects of this Center. Breast Cancer survivors are utilized as Patient Advocates for Research Participation (PARPS), that is, as recruiters. Once a case or control has been identified, she is contacted by an interviewer or PARP who schedules the first interview/assessment. Both PARPS and interviewers are culturally competent and have been fully trained. Training for the interviewers includes information on how to conduct each assessment/interview, to collect blood specimens, contact and conduct the telephone assessments for the Cases in Project 2 and the healthy adult daughters of both cases and controls for Project 3 and track their involvement across and within the project. At times, the interviewers also serve as recruiters at designated clinic sites. With the additional funding of related Department of Defense projects ('Increasing Breast Cancer Surveillance Among African American Breast Cancer Survivors' [DAMD 17-03-1-0454; SIS] and 'Immune Surveillance, Cytokines, and Breast Cancer Risk: Genetic and Psychological Influences in African American Women' [DAMD 17-02-1-0501; Cytokine Study]) the staff of the core has assisted in contacting Project 1 cases for SIS and Project 1 controls for the Cytokine Study. They have also been trained to conduct the interviews for the Cytokine Study.

BODY:

Consistent with the Statement of Work, as of this reporting period, we have addressed four major tasks. The first involves the contact of identified cases and controls by PARPS. Fourteen PARPS have been recruited and trained. A recruiter manual has been developed and is continually updated. Second, in order to complete each interview or assessment, as outlined in the Overall Program, Research Interviewers have been hired and trained to complete the interviews/assessments for each Protocol. A manual for use by interviewers has been completed and is also updated as required (including the procedures for SIS and the Cytokine Study). Since receiving HSRRB approval for Project 1, we have begun the actual fieldwork. For Project 1, we started contacting Controls from the random digit dialing (RDD) company. The third task for this Core regards the education of physicians at the cooperating hospitals. We have made contact with the cooperating hospitals and key staff at each location has been identified. Meetings have been conducted and standard procedures for the identification of cases have been established. Our Interviewers are on-site at each cooperating hospital to assist with recruiting. In addition, we have worked with the Patient Navigators/Research Nurses at the cooperating sites to ensure that they are aware of our procedures. Finally, this Core has the responsibility of tracking all of the participants in Projects 1, 2 and 3. Working with Core C, the tracking database has been completed. As SIS and the Cytokine Study have gotten HSRRB approval, the database has been modified to include these studies. Further changes are made on an as needed basis.

KEY RESEARCH ACCOMPLISHMENTS:

The following numbers are for this past grant year. For Project 1, we have collected data on 140 women. An additional 267 have been identified and are pending. For Project 2, data has been collected on 24 women, 10 are pending. For Project 3, we have completed interviews with 15 women, and have 19 pending. For the SIS study, 38 potential participants have been identified from Project 1. Out of this total, 15 women were contacted found to be ineligible or declined to participate. The remainder are pending. For the Cytokine Study, we have identified 44 potential subjects. Eleven women were found to be ineligible or were lost to follow-up. The remaining 33 are in process.

REPORTABLE OUTCOMES:

There are no results available at this time.

CONCLUSIONS:

At this point in the research, we are fully operational. All tools (assessments, tracking database, trained recruiters and interviewers) are in place and we are actively recruiting and interviewing women.

REFERENCES:

None

APPENDICES:

None

CORE B

Molecular, Diagnostics and Research Core

Core B:
Molecular, Diagnostics and Research Core

Principal Investigator: Dr. Margaret McGovern

INTRODUCTION:

The Molecular Diagnostic and Research Core of the Center for Interdisciplinary Biobehavioral Research provides expert molecular studies to identify: 1) molecular changes in two genes, BRCA 1 and 2, which are associated with breast cancer; and 2) molecular changes in DNA that are associated with variability in level of production of certain proteins that are normally found in the body that also may effect cancer risk. These analyses permit the investigators of the Center to assess the impact of these genetic factors on cancer risks, and on the psychobiology of the interaction of generic factors with family history, stress and ethnicity. The Molecular Diagnostic and Research Core investigators work with the individual project directors to identify relevant genetic risk factors, establish laboratory analyses to detect their presence in study subjects, and carry out all molecular analyses as per the individual study protocols. The Core directors are working closely with the center investigators in developing cost efficient protocols for the molecular testing.

BODY:

Task 1. To establish the methodology for the determination of the genotype of estrogen receptor genes and polymorphisms.

Allele specific oligonucleotide hybridization technology has been established in the core laboratory for genotyping for polymorphisms. This capability is routinely available and can be scaled up to handle large volumes of samples if required.

Task 2. Sequencing of BRCA 1 and 2 genes using DNA from subjects recruited from Project 2

Specimens have been received by the core laboratory and have been sequenced through an agreement with Myriad Laboratories.

Task 3. Determination of genotypes for estrogen receptor polymorphisms.

No specimens have been received by the core laboratory to date.

Task 4. Determination of the genotype for polymorphisms in TNFa

No specimens have been received by the Core Laboratory to data.

Task 5. Integration of Core laboratory into activities of training core.

The Core Laboratory professional staff provides educational sessions to trainees and investigators. The Core Laboratory Principal Investigator offered a course in the Fall 2004,

which was open to trainees and investigators. This course, entitled "Molecular for the Clinical Investigator" included a series of lectures on the application of molecular techniques in clinical investigation.

KEY RESEARCH ACCOMPLISHMENTS:
None.

REPORTABLE OUTCOMES:
The Core Laboratory has established a system for the storage and retrieval of study specimens that will safeguard confidentiality and ensure accurate retrieval. The laboratory has worked with the project PIs in the establishment of a system for the storage of specimens in a straw system.

CONCLUSIONS:
At this point in the research, no results are yet available.

REFERENCES:
None

APPENDICES:
None

CORE C

Biostatistics and Data Management Core

Core C:
Biostatistics and Data Management Core

Principal Investigator: Dr. James H. Godbold

INTRODUCTION:

The three projects in this Center project are each collecting data to address their study hypotheses. It is extremely important that the data that are collected be managed in a careful way and that the analyses that are performed on the data use statistics that lead to valid conclusions.

The objective of the Biostatistics and Data Management Core is to provide databases for entry, storage, and retrieval of data collected in the three projects of this Center. The quality of the data is monitored at each step in the process. The Core also provides statistical analyses of the data using appropriate models to address the specific aims/objectives of each project.

Without good management of data, cleaning of data to provide a valid dataset, and appropriate statistical analyses of the collected data, the work in three projects would be of little value. The members of this Core work closely with the investigators of the three projects and members of the other Cores to coordinate the data activities so that this work is done in a timely manner.

BODY/ KEY RESEARCH ACOMPLISHMENTS:

During the past year the Biostatistics and Data Management Core has modified the tracking database to facilitate the recruitment of subjects into the three Projects. Also, the databases for each of the projects' data have been finalized for receipt of completed questionnaires.

This year, data from Project 1 Questionnaires have been double entered for 120 subjects and single entered for an additional 15 women. For the women with double-entry, the two versions of entered data have been compared and the resulting discrepancies have been investigated and resolved. Data entry systems for Projects 2 and 3 have now been developed and are undergoing testing.

Flowcharts are generated bi-weekly to aid investigators in monitoring the progress of subject recruitment. The flowcharts are for the Center as a whole, as well as for each Project.

Programs have been written in SAS for data cleaning of the data collected in the questionnaires. These programs have been implemented, and queries have been generated for data items failing either range or logic checks. The status of these queries, after they have been sent to the project coordinators for resolution, is also being monitored. SAS programs for statistical analysis of the data from Project 1 have been written and tested out on a sample of the data collected thus far.

REPORTABLE OUTCOMES:

None

CONCLUSIONS:
None

REFERENCES:
None

APPENDICES:
None

CORE D

Training Core

Core D:
Training Core

Principal Investigator: Dr. Dana H. Bovbjerg

INTRODUCTION:

Breast cancer continues to be a preeminent cause of morbidity and mortality among American women, despite the recent encouraging news that cancer incidence and mortality rates have inched downward in the past decade. The risk of early mortality is a particularly a concern for African-American women. African-American women are more frequently diagnosed with advanced, aggressive tumors, and those under age 50 have nearly twice the breast cancer risk of white women. The research literature suggests that it is the interaction of behavioral and genetic factors, which may account for clinical findings among African-American women. However, few researchers today are equipped with the skills necessary to investigate the interactions among behavioral factors, genetics, and culture. The goal of the Training Core in Biobehavioral Breast Cancer Research is to foster the development of interdisciplinary researchers focused on epidemiological and biobehavioral aspects of breast cancer that are particularly relevant to African Americans through a broadly based, multidisciplinary postdoctoral training program involving a required curriculum of formal lectures, participation in specialized seminar series, "hands-on" research experience with the guidance of a nationally-recognized research mentor, and formal, as well as hands-on, training in the preparation of research papers and grants. This training will act as a bridge between behavioral and epidemiological approaches to breast cancer research.

BODY:

Because of delays waiting for HSRRB approval for Projects 1, 2, and 3, which were intended to provide direct research experience for trainees, we had to modify the timeline in our initial Statement of Work. However with the recent HSRRB approval for the Projects, we have been able to complete Tasks 1 and 2.

Tasks 1 and 3:

a) Recruit applications;
b) Evaluate potential trainees;
c) Develop and schedule Foundations Curriculum;
d) Coordinate training with ongoing Cancer Center Training Programs;
e) Schedule seminar series;
f) Run Foundations and Seminar Series;
g) Establish hands-on research experience for each Trainee;
h) Schedule and run Luncheon Lecture Series;
i) Guide development of independent research project for each Trainee;
j) Provide oversight for each Trainee's independent project;
k) Conduct formal evaluations of Trainees and Program;
l) Facilitate preparation of research reports and grant applications;

Tasks 2 and 4: Prepare and submit required reports for BCRP

Because of delays imposed by the HSRRB review, Task 1, subsections g and i-l were accomplished with related research approved by the Mt Sinai Institutional Review Board for protection of human subjects, and funded by other sources. Task 2 is completed with this report. In this past year of the grant, we have initiated Task 3, recruiting and evaluating of a second class of postdoctoral trainees. Two new trainees have begun the program and will undertake the full training program outlined in subsections c-l, with the ability to participate in the Center research projects now approved by HSSRB.

KEY RESEARCH ACOMPLISHMENTS:

Following is a sample of the training curriculum provided in the past year:

Behavioral Medicine Course (subsections c,d,f):

Introduction/Models
Stress/Concepts
Addressing Race in Health Care and Health Outcomes
Behavioral Cardiology
Obesity
Behavioral Intervention
Addiction
Mind-Body Medicine
Brain, Behavior & Immunity
Palliative Care

Work-in-Progress presentations (subsections i,l):

Predictors and Outcomes of Medical Mistrust Among African Americans and Latinos in Harlem, NYC; Dr. Hayley Thompson, Assistant Professor Oncological Sciences, MSSM

Beyond treatment decision making: Future challenges for prostate cancer survivors; Dr. Michael A. Diefenbach, Assistant Professor of Urology & Oncological Sciences, MSSM

Seminar/Lecture Series (subsections e,f,h):

Techniques in clinical research interviewing; Dr. Karen Hurley, Clinical Assistant Psychologist, Memorial Sloan Kettering Cancer Center

A Reasoned Action Approach to Health Promotion; Dr. Martin Fishbein, Professor of Communications, Annenberg School for Communication, University of Pennsylvania

REPORTABLE OUTCOMES:

Listed below are research articles by our first class of trainees published during and after the training period.

DR. NAA OYO A. KWATE: Dr. Kwate received a Ph.D. in Clinical Psychology from St. John's University in New York. Her research has focused on health disparities in cancer prevention and control. Dr. Kwate is now an Associate Research Scientist at the Mailman School of Public Health, Columbia University.

Kwate, N.O.A. (2001). Intelligence or Misorientation?: Eurocentrism in the WISC-III. The Journal of Black Psychology, 27(2), 221-238.

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Utsey, S.O., Walker, R.L., & Kwate, N.O.A. (2005). Quantitative research in a multicultural context: Practical applications for research with ethnic minority populations. In: Strategies for Building Multicultural Competence in Mental Health and Educational Settings. M. Constantine, & D.W. Sue, (Eds.). New York: Jossey-Bass.

Guevarra, J.S., Kwate, N.O., Tang, T.S., Valdimarsdottir, H.B., Freeman, H.P., & Bovbjerg, D.H. Acculturation and its relationship to smoking and breast self-examination frequency in African American women. Journal of Behavioral Medicine. 2005 Apr;28(2):191-9.

Thompson, H.S., Kwate, N.O.A. (In press). Genetic testing attitudes in the United States and Africa: The role of underdevelopment in perceived disadvantages and concerns about abuses. In: About Cancer in Africa. Paris: International Network Against Cancer in Africa.

Kwate, N.O.A. (in press). The heresy of African-centered psychology. Journal of Medical Humanities.

DR. ANNE FATONE: Dr. Fatone received a Ph.D. in Clinical & Health Psychology from Yeshiva University in New York, NY. Her research has focused on the effects of psychosocial factors in participation of medical minority populations in cancer prevention efforts. Dr. Fatone is now an Instructor at the Mount Sinai School of Medicine.

Thompson HS, Wahl E, Fatone A, Brown K, Kwate NOA, Valdimarsdottir H. Enhancing the readability of materials describing genetic risk for breast cancer. Cancer Control. 2004 Jul-Aug;11(4):245-53.

Fatone, A., Jandorf, L., Modibo Baker, J., Brenner, B., Butts, G., Cornbill, R., Itzkowitz, S.H., Levin, M., Rothenberg, A., Sacks, H., Weeks, M., Redd, W.H. (submitted). East Harlem Partnership for Cancer Awareness (EHPCA): collaborative cancer screening and prevention research in an urban minority community.

CONCLUSIONS:

We have conducted a broad-based postdoctoral training program to prepare two Trainees for interdisciplinary research in biobehavioral approaches to breast cancer. The Trainees have gone on to pursue independent research careers investigating biobehavioral processes involved in cancer and their interactions with minority culture. As we continue the training program with our newest recruits, we anticipate that they will add even more to the literature on addressing some of the more critical minority issues in biobehavioral aspects of cancer with potential clinical implications for prevention, screening, diagnosis, treatment, and survival in this underserved population.

REFERENCES:

None

APPENDICES:

None